REMARKS

Status of the Claims

Claims 1-20 were rejected. Claim 13 has been canceled without prejudice or disclaimer. Claim 1 has been amended. Claims 1-12 and 14-20 remain pending.

Claim 1 was amended to more clearly define and distinctly claim the instant invention. No new matter was entered by way of these amendments.

The Rejection of the Claims Under 35 U.S.C. §112, Second Paragraph, Should Be Withdrawn

Claims 16-20 stand rejected under 35 U.S.C. § 112, second paragraph, for indefiniteness. This rejection is respectfully traversed. The Examiner asserts that the term "subject" would not be clearly understood by one of skill in the art. While Applicants maintain that the claim term is clear, to expedite prosecution, claims 16-20 were amended in the Amendment and Response of February 1, 2005 to recite a "patient." Support this amendment can be found in the originally filed claims and on page 5, lines 6-7 of the specification. In view of the amendment, the Examiner is respectfully requested to withdraw the rejection of claims 16-20 under 35 U.S.C. §112, second paragraph.

The Rejection of the Claims Under 35 U.S.C. §102 Should Be Withdrawn

I. Claims 1-13 and 15-20 were rejected under 35 U.S.C. §102(b) as being anticipated by Roof *et al.* (1997) *Molecular and Chem. Neuropathology* 31:1-11 and claims 1-13 and 16-20 were rejected as being anticipated by Roof *et al.* (1992) *Restoration of Neurology and Neuroscience* 4:425-427. Each of these rejections is respectfully traversed.

Roof *et al.* (1992) teach the administration of progesterone to rats following a frontal contusion reduces brain edema. Roof *et al.* (1997) administered progesterone to rats following a frontal contusion and found that approximately one-third of 8-isoPGF$_{2\alpha}$ found in control rats. Roof *et al.* (1997) asserts that this data supports that progesterone has antioxidant effects. None

of these references by Roof *et al.* teach or suggest the administration of allopregnanolone to treat a traumatic CNS injury or reduce neurodegeneration following a traumatic CNS injury.

The Examiner asserts that allopregnanolone is an old and well-known progesterone metabolite, which was necessarily produced in the patient's body upon ingestion of progesterone in the body and thereby concludes that "Roof's steps are thus the same as the instant method steps..." (page 4, paragraph 3 of 11/04/04 Office Action). In support of this position, the Examiner cites *Schering Corp. v. Geneva Pharmaceutical, Inc.*, 68 USPQ 2d 1760 (CAFC 2003). It is presumed that the Examiner intended to cite *Schering Corp. v. Geneva Pharmaceutical, Inc.*, 67 USPQ 2d 1164 (Fed. Cir. 2003). As outlined below, the claims of the instant invention are not inherently anticipated by Roof *et al.* (1997) or Roof *et al.* (1992).

First, the cited case law is not applicable to the scenario at hand. The relevant issue in *Schering Corp. v. Geneva Pharmaceutical, Inc.* was whether a composition claim drawn to a metabolite was novel in view of the disclosure of the parent compound. The court found that the composition claims drawn to the metabolite were anticipated by the parent compound since, the parent compound, upon administration to a subject, would be broken down into the recited metabolite. However, the court noted that with proper claiming, patent protection is available for metabolites of known drugs. In fact, the court even provides examples of claiming strategies that would prove successful in overcoming the disclosure of the parent compound: "The patent drafter could claim a method of administering the metabolite or the corresponding pharmaceutical composition." *Schering Corp. v. Geneva Pharmaceutical, Inc.* 67 USPQ 2d 1664 (Fed. Cir. 2003) at 1670.

In the instant case, the claims of the present invention are <u>not</u> drawn toward the metabolite allopregnanolone, but rather a drawn to a novel use of the metabolite. The Roof *et al.* references teach only the administration of progesterone to a subject to treat a traumatic brain injury. The claims of the instant invention recite the "administration of a pharmaceutical composition comprising a therapeutically effective amount of allopregnanolone." A valid inherent anticipation rejection requires that every element recited in method claims 1-13 and 15-20 of the present application must be present in the method disclosed in Roof *et al.* This is simply not the case. Roof *et al.* only administers the parent compound progesterone and, as

such, does not anticipate the instant claims which recite the administration of a pharmaceutical composition comprising allopregnanolone. In view of the Examiner's suggestion set forth in the February 8, 2005 interview, claim 1 has been amended to more clearly recite that the pharmaceutical composition comprises allopregnanolone.

As claims 1-12 and 15-20 are not anticipated by the cited art, and the Examiner is respectfully requested to withdraw the rejection of the claims under 35 U.S.C. §102.

II. Claims 1-7, 13, and 16-17 were rejected under 35 U.S.C. §102(b) as being anticipated by Gee *et al.* (RE 35,517). The Examiner asserts that Gee *et al.* teaches the use of allopregnanolone for treating seizure disorders and cites Hernandes *et al.* (1997) *Neurology 48*:803-803 as teaching that "seizures are known to result from traumatic brain injury." The Examiner concludes that Gee *et al.* is teaching the administration of allopregnanolone to the same patient population as set forth in claims 1-7, 13 and 16-17. This rejection is respectfully traversed.

Gee *et al.* suggests methods of modulating brain excitability to alleviate stress, anxiety, and seizure activity. However, the claims of the instant invention are drawn to "a method of treating a *traumatic central nervous system injury*" (claims 1-15), and "a method of decreasing neurodegeneration on a population of cells in a subject *following a traumatic injury to the central nervous system*" (claims 16-20). As stated on page 6, lines 17-23 of the specification, "[a] traumatic injury to the CNS is characterized by a *physical impact* to the central nervous system" (emphasis added). Gee *et al.* does not teach or suggest administering any progesterone metabolite to a subject following a traumatic injury (i.e., physical impact) to the CNS. Contrary to the conclusions in the Office Action, the same patient population is not being treated. As the art never taught or suggested the administration of allopregnanolone to a subject having a *traumatic* CNS injury, the claims of the instant invention are not inherently taught by Gee *et al.*

The Examiner further cites Hernandez *et al.* as teaching that "seizures are known to result from traumatic brain injury." This reference offers no support to the inherent anticipation rejection. Hernandez *et al.* does teach that post-traumatic epilepsy does occur. However, the fact that post-traumatic epilepsy does occur is irrelevant to the issue at hand. Gee *et al.* does not teach the administration of allopregnanolone to a subject following a *traumatic brain injury* and

accordingly a distinct population is being treated. Per the Examiner's suggestion set forth in the February 8, 2005 interview, claim 1 has been amended to more clearly recite the patient population being treated. Accordingly, claims 1-12 and 14-20 are not anticipated by Gee *et al.*, and the rejection of the claims under 35 U.S.C. §102(b) should be withdrawn.

III. In rejecting the claims under 35 U.S.C. §102, the Examiner states on page 7, lines 1-4 of the November 4, 2004 Office Action that "Gee et al. also discloses that the beneficial effect of progesterone is related to the conversion of progesterone to the active metabolites including allopregnanolone since the metabolites and derivatives possess higher potency and efficacy than progesterone." As outlined in the part 4(a) of the declaration by Dr. David Wright filed under § 1.312 on December 19, 2003, the Examiner's statement is not accurate. For the Examiner's convenience the comments from Dr. Wright are reproduced below:

> Gee *et al.* teach that both progesterone and many of its metabolites bind with high affinity to a unique GABA/GBR complex and that these metabolites delay onset of myoclonus following TBPS induced seizures in mice. There is no data demonstrating that progesterone and allopregnanolone are effective at treating other disease states, such as traumatic brain injury, and certainly no teaching that *all* of progesterone's beneficial effects are related to progesterone's conversion into its various metabolites.

IV. Claims 1-7, 12-13 were rejected under 35 U.S.C. §102(b) as being anticipated by Tauboll *et al.* (1993) *Epilepsy Research 14*:17-30. This rejection is respectfully traversed.

Tauboll *et al.* teach that administration of allopregnanolone increases the seizure threshold in a dose dependant manner when seizures were produced via an electrical stimulation in the primary visual cortex of a cat. The cats employed by Tauboll *et al.* did not suffer a "physical impact" and accordingly, the reference does not teach the administration of allopregnanolone following a traumatic injury as recited in claims 1-7 and 12-13. Once again, the patient population being treated by Tauboll *et al.* is not the same as the patient population recited in the instant claims. Per the Examiner's suggestion set forth in the February 8, 2005, claim 1 has been amended to more clearly recite the patient population being treated.

Accordingly, claims 1-7 and 12-13 are not inherently anticipated by Tauboll *et al.*, and the Examiner is respectfully requested to withdraw the rejection of the claims under 35 U.S.C. §102.

The Rejection of the Claims Under 35 U.S.C. §103 Should Be Withdrawn

Claim 4 was rejected under 35 U.S.C. §103 as being unpatentable over Roof *et al.* or Gee *et al.* in view of U.S. Patent 5,068,226 (Weinshenker *et al.*). This rejection is respectfully traversed.

Claim 4 recites a method of treating a traumatic central nervous system injury comprising administering to a patient in need thereof a therapeutically effective amount of a pharmaceutical composition comprising allopregnanolone, wherein said method reduces edema in the patient following said traumatic CNS injury. As the Examiner's comments on page 9 of the November 4, 2004 Office Action relate to the use of cyclodextrins, Applicants assume the Examiner intended to reject claim 14 which recites that the carrier is cyclodextrin. Applicants address their comments below to claim 14.

An obviousness rejection requires that the cited references teach all of the claim limitations. As discussed above, none of the cited references teach the administration of allopregnanolone to a subject following a traumatic CNS injury. As such, a *prima facie* case of obviousness has not been made, and the rejection of claim 14 under 35 U.S.C. §103 should be withdrawn.

CONCLUSIONS

In view of the foregoing amendments and remarks, Applicants respectfully submit that the rejections of claims 1-12 and 14-20 under 35 U.S.C. § 112, second paragraph, 102, and 103 have been overcome. Accordingly, Applicants submit that this application is in condition for allowance. Early notice to this effect is solicited.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required

therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,

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